

CLAIMS

1. A non-human transgenic animal having a transgene comprising a polynucleotide sequence encoding a fusion protein which activates transcription, the fusion protein
5 comprising a first polypeptide which binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which activates transcription in eukaryotic cells.
2. The animal of claim 1, wherein the first polypeptide of the fusion protein is a mutated
10 Tet repressor.
3. The animal of claim 2, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.
- 15 4. The animal of claim 3, wherein the mutated Tet repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102.
- 20 5. The animal of claim 4, wherein the mutated Tn10-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.
6. The animal of claim 1, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.
- 25 7. The animal of claim 1, further having a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.
8. The animal of claim 7, further having a third transgene comprising a polynucleotide sequence encoding a fusion protein which inhibits transcription, the fusion protein
30 comprising a first polypeptide which binds to a *tet* operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells.
9. The animal of claim 1, which is a mouse.
- 35 10. The animal of claim 1, which is selected from a group consisting of a cow, a goat, a sheep and a pig.

11. A method for modulating transcription of the second transgene in the transgenic animal of claim 7, comprising administering tetracycline or a tetracycline analogue to the animal.

5 12. A non-human transgenic animal having a transgene comprising a polynucleotide sequence encoding a fusion protein which activates transcription, the fusion protein comprising a first polypeptide which binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which
10 predetermines location within a chromosome within cells of the animal.

13. The animal of claim 12, wherein the first polypeptide of the fusion protein is a mutated Tet repressor.

15 14. The animal of claim 13, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

15. The animal of claim 14, wherein the mutated Tet repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one amino acid position selected
20 from the group consisting of position 71, position 95, position 101 and position 102.

16. The animal of claim 15, wherein the mutated Tn10-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.

25 17. The animal of claim 12, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

18. The animal of claim 12, further having a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

30 19. The animal of claim 18, further having a third transgene comprising a polynucleotide sequence encoding a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a *tet* operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells.

35 20. A method for modulating transcription of the second transgene in the transgenic animal of claim 18, comprising administering tetracycline or a tetracycline analogue to the animal.